

REMARKS

Upon Amendment, Claims 3-6, 8, 9, and 20-30 are currently pending in this application. Previously withdrawn claims 1, 2 and 10-19 have been canceled without prejudice or disclaimer. Claims 3, 4, 8, 9, 24 and 25 have been amended. Claims 26-30 have been added and are directed to the methods of the presently elected invention utilizing the additional specifically disclosed species as outlined by the examiner (i.e., at least one additional opioid analgesic selected from the group consisting of morphine-6- glucuronide, 6-acetylmorphine, and codeine.) As Applicant believes the elected species Morphine will be found allowable with this amendment, Applicant respectfully requests the Examiner to expand the search to include the other disclosed species.

Support for the claim additions and amendments can be found throughout the specification and claims as originally filed. No new matter has been added.

Amendment and cancellation of the claims herein are not to be construed as acquiescence to the rejections/objections set forth in the Final Office Action and/or any previous office action and were done solely to expedite prosecution of the application. Applicant hereby reserves the right to prosecute the claims as originally filed or similar claims in this application or one or more subsequent patent application.

Reconsideration and withdrawal of the objections to this application in view of the remarks herewith, are respectfully requested, as the application is in condition for allowance.

Applicants respectfully thank the Examiner for the acknowledgement of the priority of the instant application and the withdrawal of the anticipation rejections over Bolan and Smith and the obviousness rejection over Bolan.

Statement of Substance of Interview

Applicant wishes to thank Examiners Karol and Kim for the courteous and helpful telephone interview held on June 30, 2009 with Applicant's undersigned representative; Assignee's Representative, Jeanne Farrell; and Inventor Gavril Pasternak. During the interview, the art cited in the Final Office Action mailed was discussed. The Examiner recognized Applicant's position that

the effect of the combination of methadone and morphine in Smith is less than that of morphine alone.

Furthermore, Applicant discussed the general state of the art for using combination therapies; specifically, that one of ordinary skill in the art at the time of the invention would have been motivated to use a combination of therapies which have differing modes of action and that one of ordinary skill would not have had motivation to utilize two opioids. Nevertheless, the Applicant has demonstrated a synergistic effect using L-methadone and, at a minimum, the opioids of Table 1 (specification, page 15). No final agreement as to the allowability of the claims was reached.

Rejections under 35 U.S.C. §103 (a)

Claims 3-9 and 20-25 are rejected under 35 U.S.C. §103(a) as being obvious over Smith in view of United States Patent No. 6,008,258 to Inturrisi ("Inturrisi"). Applicant respectfully traverses the rejection.

Applicant has previously argued that Smith does not teach or suggest the administration of enantiomerically pure L-methadone or a mixture of D- and L- methadone having at least 65% L-methadone. Applicant further asserts that Smith teaches away from the combination of morphine and methadone. Furthermore, Applicant has demonstrated a surprising and unexpected synergy with respect to the combination of L-methadone and certain opioid analgesics.

Applicant respectfully notes that "It is improper to combine references where the references teach away from their combination...(The claimed catalyst which contained both iron and an alkali metal was not suggested by the combination of a reference which taught the interchangeability of antimony and alkali metal with the same beneficial result, combined with a reference expressly excluding antimony from, and adding iron to, a catalyst.)." M.P.E.P §2145 citing *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983).

Applicant respectfully invites the Examiner's attention to Page 337 of Smith which states "no additive effects were obtained following combined administration of methadone and morphine.

Throughout the observation period the average reaction time of the group receiving both ... methadone and ... morphine was less than that of the group receiving the same dose of morphine alone.” As Applicant discussed during the telephonic interview, one of ordinary skill in the art would readily understand this passage of Smith to mean that not only did the combination of methadone and morphine not result in an effect, which would have been expected from the combination (i.e. an additive), but also the combination in fact had a less desirable effect than using morphine alone. This represents a clear teaching away from the combination of methadone and morphine

Applicant further asserts that, prior to the present invention, the common strategy of one of ordinary skill in the art of combination therapy, was to utilize two or more drugs of different mechanisms so as to reduce potential side effects.

As previously argued, Inturrisi, which is related to the treating tolerance and physical dependence in a subject having a NMDA receptor using d-methadone, does nothing to rectify the deficiencies of Smith in light of the general knowledge of the art.

In light of this common knowledge and the teaching away of Smith, Applicant contends that one of ordinary skill in the art would have had no motivation to combine methadone with morphine, or any other opioid analgesic without potentially reducing the efficacy of both drugs. Similarly, even if one had combined L-methadone with another opioid analgesic, one of ordinary skill in the art would have lacked any reasonable expectation of success as Smith clearly shows the combination results in a lessening effect as opposed to the synergistic effect of the present invention.

With regard to the unexpected properties demonstrated by the Applicant in the Specification and in the prior arguments, Applicant respectfully disagrees with the Examiner’s statement on page 5 of the Office Action that the data presented is not commensurate with the scope of the claims. As previously stated, in Example 1 (specification, page 15), Applicant provides a table which shows the relative potency of L-methadone, D-methadone, morphine, M6G, codeine, 6-acetylmorphine and fentanyl using a radiant heat tail-flick assay. The combination of L-methadone with each drug resulted in a potency 3-4 times greater than the expected additive effect of the two drugs. Similarly,

in Example 2 (specification, page 16), the same test was performed with morphine in combination with the other opioids instead of L-methadone. In each case, only additive effects were observed. Finally, in Example 3 (specification, page 17), Applicant showed that even at a dose 8 times higher than that of L-methadone, D-methadone did not have an influence on the morphine response whereas the L-methadone combination showed a 3-4 times greater effect. As such, Applicant believes that the data presented is commensurate in scope with the present claims.

Applicant respectfully submits that rejection under 35 U.S.C. §103(a) should be withdrawn.

CONCLUSION

In view of the remarks made herein, Applicant submits that the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. If a telephone conference with Applicant's representative would be helpful in expediting prosecution of the application, Applicant invites the Examiner to contact the undersigned at the telephone number indicated below.

Applicant believes that no additional fees, other than the fee for the three-month extension of time, are required in connection with this paper. Nevertheless, Applicant authorizes the Director to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 04-1105, under Order No. 62076(51590).

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Respectfully submitted,

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